

WHAT IS CLAIMED IS

1. A pharmaceutical composition comprising an orally administrable effective unit dosage of a primary N-hydroxylamine, or corresponding nitron prodrug thereof, or a pharmaceutically acceptable salt thereof, wherein the hydroxylamine has the general formula,



wherein R₁, R₂ and R₃ are independently selected from: hydrogen, substituted or unsubstituted (C1-C10) alkyl, alkenyl, alkynyl, aryl, oxyl, acyl, carboxyl, amino, nitro, nitroso, oxime, hydrazone, azo, thiol, sulfonyl and halide,

 wherein the composition is packaged with a label identifying the primary N-
10 hydroxylamine and prescribing a pharmaceutical use thereof and the use comprises reducing oxidative damage or delaying senescence.

2. A composition according to claim 1, wherein the dosage is from 100ug to 1g.

15 3. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is selected from unsubstituted (C1-C10) alkyl, alkenyl and alkynyl.

4. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is selected from unsubstituted (C1-C18) alkyl, cycloalkyl, alkenyl and alkynyl, and the R is selected from:

20 $\text{CH}_3-(\text{CH}_2)_{n_1}$, $(\text{CH}_3-(\text{CH}_2)_{n_2})_2 \text{CH}$, $(\text{CH}_3-(\text{CH}_2)_{n_2})_3$, cyclopentyl, cyclohexyl, $(\text{CH}_2=\text{CH}-\text{CH}_2)_{n_3}$ and $(\text{CH}\equiv\text{C}-\text{CH}_2)_{n_3}$, wherein $n_1 = 1$ to 18, $n_2 = 1$ to 17 and $n_3 = 1$ to 3.

5. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is selected from hydrogen, unsubstituted (C1-C10) alkyl, alkenyl and alkynyl, and the hydroxylamine is
25 selected from:

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| N-methylhydroxylamine, | N-(n-decahexyl)hydroxylamine, |
| N-ethylhydroxylamine, | N-(n-decaoctyl)hydroxylamine, |
| N-n-propylhydroxylamine, | N-isopropylhydroxylamine, |
| N-(n-butyl) hydroxylamine, | N-sec-butylhydroxylamine, |
| 5 N-(n-pentyl)hydroxylamine, | N-tert-butylhydroxylamine, |
| N-(n-hexyl)hydroxylamine, | N-cyclohexylhydroxylamine, |
| N-(n-heptyl)hydroxylamine, | N-cyclopentylhydroxylamine, |
| N-(n-octyl)hydroxylamine, | N-(2-propene)hydroxylamine, |
| N-(n-nonyl)hydroxylamine, | N-(3-butene)hydroxylamine, |
| 10 N-(n-decyl)hydroxylamine, | N-(2-propyne)hydroxylamine and |
| N-(n-dodecyl)hydroxylamine, | N-(3-butyne)hydroxylamine. |

6. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted aryl.

7. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted aryl, and the R is selected from: mono, di, or tri methyl, methoxy, halo, nitro, amino, hydroxyl and substituted or unsubstituted phenyl, naphthyl, anthryl, phenanthryl, pyridyl, quinoliny, imidazolyl, benzoxazolyl, pyrrolyl, furanyl, piperidinoly and tetrahydrofuranyl.

8. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted aryl, and the hydroxylamine is selected from:

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| N-benzylhydroxylamine, | N-(1,3-diaminobenzyl)hydroxylamine, |
| 25 N-(n-nitrobenzyl)hydroxylamine, | N-(1,3-hydroxybenzyl)hydroxylamine, |
| N-(n-methylbenzyl)hydroxylamine, | N-(2,4-diaminobenzyl)hydroxylamine, |
| N-(n-chlorobenzyl)hydroxylamine, | N-(2,4-dihydroxybenzyl)hydroxylamine, |
| N-(n-aminobenzyl)hydroxylamine, | Imidazole-2-methylhydroxylamine and |
| N-(n-hydroxybenzyl)hydroxylamine, | Benzoxazole-2-methylhydroxylamine, |

wherein n is selected from 1, 2, 3, 4, 5 and 6.

9. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted

or unsubstituted (C1-C18) oxyl.

10. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) oxyl and the R is selected from: hydroxyl, hydroxyalkyl (HO-(CH₂)_{n1}), hydroxyaryl selected from benzylalcohol, phenol and naphthol, alkoxy (O-(CH₂)_{n1}) and aryloxy selected from phenoxy, benzyloxy and naphthyloxy, wherein n1= 1 to 18.

11. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18)alkyl hydroxyl or arylhydroxyl and the hydroxylamine is selected from:

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| N-(hydroxymethyl)hydroxylamine, | N-(methoxymethyl)hydroxylamine, |
| N-(2-hydroxyethyl)hydroxylamine, | N-(methoxyethyl)hydroxylamine, |
| N-(3-hydroxypropyl)hydroxylamine, | N-(methoxyisopropyl)hydroxylamine, |
| N-(4-hydroxybutyl)hydroxylamine, | N-(benzyloxymethyl)hydroxylamine and |
| N-(6-hydroxyhexyl)hydroxylamine, | N-(4-hydroxymethylbenzyl)hydroxylamine. |
| N-(12-hydroxydodecyl)hydroxylamine, | |

12. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) alkylcarboxyl or arylcarboxyl.

13. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) alkyl or aryl carboxyl and the R is selected from carboxyalkyls and benzyl.

14. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylcarboxyl and the hydroxylamine is selected from:

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| N-(carboxymethyl)hydroxylamine, | N-(5-carboxypentyl) hydroxylamine, |
| N-(2-carboxyethyl)hydroxylamine, | N-(6-carboxyhexyl)hydroxylamine, |
| N-(3-carboxypropyl)hydroxylamine, | N-(4-carboxybenzyl)hydroxylamine and |
| N-(4-carboxybutyl)hydroxylamine, | N-(12-carboxydodecyl)hydroxylamine. |

15. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted

or unsubstituted (C1-C18) ester.

16. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) ester and the R is selected from alkyl (C1 – C18) and aryl esters.

17. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylesters and the hydroxylamine is selected from:

N-(acetyloxymethyl)hydroxylamine,

N-(acetyloxyethyl)hydroxylamine,

N-(acetyloxypropyl)hydroxylamine,

N-(propylcarbonyloxy)methylhydroxylamine,

N-(butylcarboxyloxy)methylhydroxylamine,

N-(tert-butyloxycarbonyl)methylhydroxylamine,

N-(benzyloxycarbonyl)methylhydroxylamine,

N-(phenyloxycarbonyl)methylhydroxylamine,

N-(3-pyridyloxycarbonyl)methylhydroxylamine and

N-(benzoxazol-5-carbonyloxy)methylhydroxylamine.

18. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) carbonyl.

19. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted carbonyl and the R is selected from alkyl (C1 – C18) carbonyls and aryl carbonyls.

20. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylcarbonyls and the hydroxylamine is selected from:

N-(acetyl)methylhydroxylamine,

N-(phenylcarbonyl)methylhydroxylamine

N-(ethylcarbonyl)methylhydroxylamine,

and

N-(butylcarbonyl)methylhydroxylamine,

N-(benzylcarbonyl)methylhydroxylamine.

21. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted

or unsubstituted alkyl(C1-C18) or aryl amino.

22. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or aryl amino and the R is selected from primary alkyl amine selected from methylamine, ethylamine, propylamine, butylamine and hexylamine, secondary amine selected from dimethylamine, diethylamine and dipropylamine, tertiary amine selected from trimethyl and triethylamine, and quarternary amine selected from tetramethyl and tetraethylammonium salts.

23. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted alkyl(C1-C18) or aryl amine and the hydroxylamine is selected from:

N-aminomethylhydroxylamine,
N-(2-aminoethyl)hydroxylamine,
N-(N-methylamino)methylhydroxylamine,
N-(N,N-dimethylamino)methylhydroxylamine,
N-(N,N,N-trimethylammonium)methylhydroxylamine,
N-(3-aminopropyl)hydroxylamine,
N-(6-aminohexyl)hydroxylamine,
N-(4-aminobenzyl)hydroxylamine,
Hydroxylamine –1-methylpyridinium and
Hydroxylamine-1-methylquinolinium.

24. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) alkyl or aryl nitro.

25. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted alkyl(C1-C18) or aryl nitro and the R is selected from alkyl nitro selected from nitromethyl, nitroethyl, nitropropyl, nitrobutyl, nitropentyl, nitrohexyl and nitrobenzyl, and aryl nitro selected from nitrophenyl and nitronaphthyl.

26. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or aryl nitro and the hydroxylamine is selected from:

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| N-(nitromethyl)hydroxylamine, | N-(5-nitropentyl)hydroxylamine, |
| N-(2-nitroethyl)hydroxylamine, | N-(6-nitrohexyl)hydroxylamine, |
| N-(3-nitropropyl)hydroxylamine, | N-(4-nitrobenzyl)hydroxylamine and |
| N-(4-nitrobutyl)hydroxylamine, | N-(2,4-dinitrobenzyl)hydroxylamine. |

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27. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) nitroso.

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28. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) nitroso and the R is selected from aliphatic nitrosoamines and aromatic nitroso.

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29. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted nitroso (C1-C18) and the hydroxylamine is selected from:

N-(N-methyl-N-nitroso-amino)methyl hydroxylamine,
 N-(N-methyl-N-nitroso-2-amino)ethylhydroxylamine,
 N-(N-methyl-N-nitroso-3-amino)propylhydroxylamine and
 N-(p-nitroso)benzylhydroxylamine.

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30. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted oxime.

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31. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) oxime and the R is selected from: acetaldoxime, propionaldoxime, butanaldoxime and benzaldoxime.

32. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted oxime (C1-C18) and the hydroxylamine is selected from:

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| Acetaldoxime-3-hydroxylamine, | Butanaldoxime-5-hydroxylamine and |
| Propionaldoxime-4-hydroxylamine, | (4-benzaldoxime)1-methylhydroxylamine. |

33. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted

or unsubstituted (C1-C10) hydrazone.

34. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C10) hydrazone and the R is selected from: acetaldehyde hydrazone, propanaldehyde hydrozone, butanaldehyde hydrazone and phenylhydrazone.

35. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted hydrazone (C1-C10) and the hydroxylamine is selected from

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| 1-hydroxylamine-acetaldehyde hydrazone, | 1-hydroxylamine-butanaldehyde hydrazone |
| 1-hydroxylamine-propanaldehyde | and |
| hydrazone, | 1-hydroxylamine-benzylaldehyde |
| | hydrazone. |

36. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted azo.

37. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted azo and the R is selected from: azobenzene, p-(phenylazo)benzyl and p-diazobenzyl.

38. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted azo and the hydroxylamine is selected from:

N-(p-phenylazo)benzylhydroxylamine,
N-(p-diazobenzyl)hydroxylamine and
N-(p-methoxyphenylazo)benzylhydroxylamine

39. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) thiol.

40. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) thiol and the R is selected from (C1-C18) alkylthiol selected from methyl, ethyl, propyl, butyl, pentyl and hexyl thiol, and arylthiol selected from thiophenol

and benzylthiol.

41. A composition according to claim 1, wherein at least one of R_1 , R_2 and R_3 is substituted or unsubstituted (C1-C18) thiol and the hydroxylamine is selected from:

N-(thiomethyl)hydroxylamine, N-(3-thiopropyl)hydroxylamine and
N-(2-thioethyl)hydroxylamine, N-(p-sulfhydryl)benzylhydroxylamine.

42. A composition according to claim 1, wherein at least one of R_1 , R_2 and R_3 is substituted or unsubstituted (C1-C18) sulfonic acid.

43. A composition according to claim 1, wherein at least one of R_1 , R_2 and R_3 is substituted or unsubstituted (C1-C18) sulfonic acid and the R is selected from methanesulfonic acid, ethanesulfonic acid, propanesulfonic acid, butanesulfonic acid and p-toluenesulfonic acid.

44. A composition according to claim 1, wherein at least one of R_1 , R_2 and R_3 is substituted or unsubstituted (C1-C18) sulfonic acid and the hydroxylamine is selected from:

1-hydroxylamine-methanesulfonic acid, 1-hydroxylamine-butane-4-sulfonic acid
1-hydroxylamine-ethane-2-sulfonic acid, and
1-hydroxylamine-propane-3-sulfonic acid, N-(p-sulfobenzyl)hydroxylamine.

45. A composition according to claim 1, wherein at least one of R_1 , R_2 and R_3 is halide.

46. A composition according to claim 1, wherein at least one of R_1 , R_2 and R_3 is halide and the R is selected from F, Cl, Br and I.

47. A composition according to claim 1, wherein at least one of R_1 , R_2 and R_3 is halide and the hydroxylamine is selected from:

N-(chloromethyl)hydroxylamine, N-(4-chlorobutyl)hydroxylamine,
N-(bromomethyl)hydroxylamine, N-(p-chlorobenzyl)hydroxylamine,
N-(2-chloroethyl)hydroxylamine, N-(p-fluorobenzyl)hydroxylamine and
N-(3-chloropropyl)hydroxylamine, N-(p-iodobenzyl)hydroxylamine.

48. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted hydroxylamine.

49. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted hydroxylamine and R is selected from N-methylhydroxylamine, N-ethylhydroxylamine, N-propylhydroxylamine N-butylhydroxylamine, N-pentylhydroxylamine, and N-benzylhydroxylamine.

50. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted hydroxylamine and the hydroxylamine is selected from:

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| Bis-methylhydroxylamine, | Bis-(3-propyl)hydroxylamine and |
| Bis-(2-ethyl)hydroxylamine, | Bis-benzylhydroxylamine. |

51. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester.

52. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester and the R is selected from: dimethylphosphate, diethylphosphate, dipropylphosphate and benzylphosphate.

53. A composition according to claim 1, wherein at least one of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester and the hydroxylamine is selected from:

di-hydroxylaminemethylphosphate ester,
mono-hydroxylaminemethylphosphate ester,
mono-(1-hydroxylamine)-ethyl-2-phosphate ester,
di-(1-hydroxylamine)-2-ethylphosphate ester,
di-(1-hydroxylamine)-3-propyl-phosphate ester,
mono-(hydroxylamine-benzyl-phosphate ester and
di-hydroxylamine-benzylphosphateester.

54. A composition according to claim 1 further comprising an effective amount of a carnitine.

55. A method for reducing oxidative damage to, or delaying senescence of a cell comprising the step of contacting a cell subject to or at risk of undesirable oxidative damage or senescence with a composition according to claim 1.

5 56. A method for reducing oxidative damage to, or delaying senescence of a cell comprising the steps of:

identifying a cell as subject to or at risk of undesirable oxidative damage or senescence; and

contacting the cell with a composition according to claim 1.

10 57. A method according to claim 56, wherein the cell is contained in other than a cancerous host.